ON

ARTIFICIAL TUBERCULOSIS,

AND ITS RELATION TO

CELLULAR PATHOLOGY AND THE GROWTH OF TUMOURS.

BY

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ON ARTIFICIAL TUBERCULOSIS.[1]

It has been said, "The different steps in attaining knowledge are marked by the acquirement of new laws or rules, expressing that to the whole of a given class of things some mark or property belongs"—and that "whenever things are really definite, as having some marks that group them into a smaller group by themselves, science requires that instead of appearing as part of a larger class, they should have their own name and position."[2]

True as these remarks are when applied to the exact science of thought, they are not the less applicable to that of medicine, since few there are who do not in their earlier years of study and practice frame for themselves certain general laws, which, as experience becomes larger, the insight into the workings of disease somewhat deeper, and the appreciation of minute variations in the conditions of the state called health more real, gradually recede into the background, displaced by the countless exceptions which would appear to put all laws at defiance, and to extinguish the hope, should any yet remain, of ever attaining to a perfect system in medicine.

"Knowledge brings doubts and exceptions and limitations which, though occasionally some aids to truth, are all hindrances to vigorous statement."[3]

Every day the tendency is more and more to make the mind a *note-book* of individual cases, which may serve as standards of comparison, rather than a compendium of rules to be slavishly adhered to. Thus is everything called by its own name, each single case has its own pathology wherein it differs from others of its class, and classification is by this means practically ignored.

While, however, from such an analytical process the life-history of disease is clearly traced, and the links in each chain are gradually ranged in proper order, it is possible that attention, concentrated on minute particulars, may narrow our conceptions of any subject as a whole, and by so doing we may miss entirely the real import of symptoms and pathological conditions, and elaborate an error in the search for truth. In disease, as elsewhere, primary and secondary causes cannot be considered apart; coexisiting phenomena must receive their due value as modifying agents, the warp and the woof of the web must be unravelled together; if otherwise, the fabric is spoiled. Thus has it been with the product tubercle, which, during the last few years, has been so prominently and frequently under discussion. In studying it we were in great danger of losing our-

[1] Being the substance of an essay which obtained honours at the Medical Graduation at Aberdeen, in April 1871.

[2] An Outline of the Laws of Thought. By Archbishop Thompson, F.R.S., etc.

[3] Companions of my Solitude, 6th ed., p. 21.

selves in detail and minutiæ, because, omitting to reflect upon the results of our investigations, we did not notice to what end they pointed. Latterly, however, important clinical and pathological facts have been brought forward, helping to point out the relationship of tubercle to other morbid products, but additional evidence is still wanting ere it can be rescued finally from the time-honoured category of *unorganizable fibrinous exudations*. It is my object to bring forward some such evidence in this paper; and though the ideas embodied in it may not open up any new line of thought, they will, I think, inasmuch as they are the result of independent experiment and observation, strengthen somewhat the position of those who have already pushed the doctrine of artificial tuberculosis to what must be considered their legitimate conclusions, and help towards obtaining for the tuberculous state its true position in a pathological scheme, as the connecting link, so to speak, when viewed with its surroundings, between various diverse morbid conditions.

In the first place, then, what is tubercle?

All the older writers on this disease may be classed in three groups; of which one, including Rokitansky, Bennett, Ancell, and Lebert, declares it to be a low formed exudation; a second, to which belong Williams, Henle, and Addison, that it is a retrograde metamorphosis of pre-existing tissues; while MM. Lallemand, Cruveilhier, and Andral considered it to be a concrete form of pus. Opinions were thus divided till M. Villemin published his "Researches on the Inoculation of Tubercle," in 1865. Those experiments I afterwards repeated myself, making use of blood, pus, tubercular sputa, cheesy matter from tubercular ulcers, cancer juice, etc., for the inoculation. It is quite unnecessary to give a detailed account of these here, now that the results of similar experiments are well known; suffice it to say, that my own observations completely coincide with those of Drs Burdon Sanderson, and Wilson Fox, published after most of mine were made,[1] and which show that—

1*st*, Tuberculosis may be with certainty produced both in the rabbit and guinea-pig (in the dog also, according to Cohnheim), either by the production of an abscess in any part of the body, by the introduction of foreign matter under the skin, or by injecting pus, tubercular matter, etc., directly into one of the serous cavities.

2*dly*, The new product tubercle is a formation of tissue composed of large numbers of lymph-like corpuscles and nuclei embedded in alveolar spaces.

[1] Dr Alison, of Edinburgh, had, as early as 1829, published the results of some experiments made by Dr Kay, at the Royal Infirmary, in which the introduction of mercury into the trachea of the dog had produced an apparent tuberculosis. In the centre of each tubercle, however, a small globule of mercury was found. This probably made the results appear less conclusive than they would have been, had the foreign matter been distant from the secondary tuberculosis; and to this cause may probably be attributed the fact, that these did not awaken that amount of discussion to which they were certainly entitled.

I wish also to insist on the fact, that the disease attacks the animal in one of two ways—either by direct contact of the morbid material with a secreting surface, on which it can engraft itself, which may be called primary infection; or else, by the production of a cold abscess, to borrow the phrase, it extends along the lymphatics, the system being affected secondarily as the result of the abscess. The former plan generally obtains where pus or contagious matter is brought into direct contact with the pleura or peritoneum. Thus, in one of my experiments, some pus expectorated by a patient affected with tuberculosis was injected into the abdominal cavity of a guinea-pig; the animal died in thirteen days' time, and I found general miliary tuberculosis of the omentum and mesentery. The solid organs and the lungs only showed signs of commencing disease. The second method is ordinarily seen when a subcutaneous inoculation has been made.

The ultimate microscopical appearance of this new, or adenoid material, as it is called, is the same in all the tissues attacked by it, whether it be produced artificially or otherwise; but the details of its progress vary somewhat, according to the site of the disease, and the mode of its onset. By the so-called primary infection, a direct process of seed-sowing and growth takes place. By the secondary, a more complex method is necessitated.

Thus, in the brain, as is well known, the new formation occupies the lymphatic spaces immediately around the vessels, and is nothing more than an excessive development of the cells normally existing there. In the omentum also, much the same process goes on. I find similar lymphatic spaces existing in large numbers, and the growth commences within these, as in the brain, immediately outside the vessels. From within it spreads to the glands and fat-depots immediately outside the perivascular spaces (possibly this may be brought about, as I have reason to think it may be, in inflammatory conditions, by the molecular disintegration of the fat-cells), the lymphoid cells gradually increase in number, till at last the adipose matter entirely disappears, and what are known as tubercles are found.

Thus far, then, be it observed, the disease is confined to the vessels and parts immediately outside them, to the network itself, while the meshes of the net are still unattacked. The delicate connective tissue which fills in these spaces appears to be invaded from the parts already attacked, and to be only a stage later than that which has already been described.

The connective tissue nuclei swell out, and, proliferating, join on to neighbouring cells, till, from the diseased structures outside the vessels, there juts out a process of swollen granular cells; this gradually extends into the parenchyma, forming, so to speak, an animal spongiole; small tubercles form on these and in their vicinity, and it seems possible that these spongioles may ultimately form lymphatic channels, after the manner of the formation of blood-vessels; but I have been unable in any instance to detect the inter-

meditate stage of partial formation of a canal. Whether the infection be primary or secondary seems then to make this difference, that, whereas in the former, where the inoculating matter is brought into direct contact with a moist secreting surface, all parts of the membrane are attacked simultaneously; in the latter, the parenchyma only suffers by a gradual process of invasion from the perivascular spaces. I have already given one illustration of the first method, in the case of a guinea-pig, where the disease was produced artificially in the omentum; let me now add another, where it occurred apparently in the same way in the brain of a child.

Case 1.—William B., æt. 19 months, was admitted to the Evelina Hospital in 1869, under Dr Hilton Fagge, with all the symptoms of tubercular meningitis. He quickly became comatose, and died in three or four days. At the post-mortem, after taking off the calvarium and dura mater, the whole surface of the brain was found to be covered with a thick layer of green pus, the same material was found at the base, a little way down the cord, and in the ventricles. On washing this away, and looking for tubercle, none was found. That is to say, no nodular growth had taken place around the vessels, as is usual in this disease; but when the membranes were examined microscopically, after being washed and stained with carmine, then multitudes of small points of adenoid growth could be seen all over the field, and localized in no one part more than another. The lungs also were scattered over with yellowish punctiform dots. No gray tubercle existed anywhere.

In the lungs, the growth takes on the same corpuscular form, and is found distending the alveolar wall. It is also accompanied by what Dr Sanderson calls *catarrhal pneumonia*, which is an increased epithelial formation from the surface of the air vesicles.

Something like this, then, is the present view of tubercle; and assuming, as indeed we believe, that it is a correct one, certain conclusions may be drawn from it:—

1*st*, That tubercle is not an exudation of fibrinous cacoplastic material, nor a retrograde metamorphosis of pre-existing tissues.

2*dly*, That it is essentially a growth[1] just as much as is any tumour, and that it is perhaps *generally*, but by no means always, an overgrowth of the elements already existing in the parts affected.

Now, what has been proved to be true in the lower animals concerning the production of tuberculosis as the effect of a caseous abscess, is probably true of man also, save that it does not follow of necessity because a patient has a chronic abscess or a suppurating sore that he must become tubercular. What I have to do, then, will be to show that such a sequence of events does at any rate occasionally take place, and to offer an explanation, if any can be

[1] Laennec calls tubercle a growth, or rather he speaks of the "growth of tubercle," but it is clear that in making use of the word, he intended to express, not that tubercle had any of the characters which we now attach to "tumour," but rather that it had a tendency to increase, that increase being a process of accretion or accumulation—a state of passivity, not of activity.

found, of those cases of prolonged suppuration in which tuberculosis does *not* occur, and also of those at first sight even more puzzling ones, in which tubercle is found unassociated with manifest suppuration or exciting cause, and which have all till lately been ascribed to diathesis.

Those last-mentioned might be disposed of at once according to Buhl,—who says that there is a *constant* dependence of miliary tubercle on pre-existing cheesy products,—did I agree with him as to the facts; but, on the contrary, looking over the post-mortem records at Guy's Hospital for 1868–9–70, I find, of 166 cases of tuberculosis, 80 or nearly half have no mention of any suppuration or cheesy glands, or anything of the kind; and though possibly this proportion is too high, and would be altered if a larger number of cases were collated, still I think some such do occur, and there is no *necessary* connexion between cheesy deposits and tubercle. One no doubt often does follow the other, but I hope to show that a simple inflammation, if continued long enough, will also end in the same way.

It will be found, then, that the cases of tuberculosis in man which come under notice fall into two classes—(*a*) Those in which it coexists with cheesy deposits; (*b*) Those in which it exists alone.

The former class, the one linked more especially with the results of our experiments, may be illustrated by the accompanying cases:—

Case 2.—William W., æt. 40, came to me as an out-patient when House Physician at Guy's Hospital. He gave this history: That he was in perfect health till four and a half months ago. He was driving a horse which suddenly reared, and his chest became crushed between the shaft and the wall of a house. He immediately brought up some blood and phlegm, and continued to do so for ten days. He was soon afterwards obliged to give up work, and began to waste. Fourteen days before admission he complained of great tenderness over the sternum, which is now hot and uneven, and has all the appearance of having been fractured. He was afterwards admitted an in-patient under Dr Moxon, and died in the Hospital. The account of the post-mortem is an abstract from the Guy's post-mortem records:—

Body much wasted. Sternum separated at the junction of the middle and lower third into two portions, and both ends are carious. There is cheesy or pasty pus extending towards the skin, and collecting there in a subcutaneous abscess. A second abscess was found in the abdominal wall of the left flank. It was encysted, and could be taken out easily. Well-marked tubercular phthisis existed in both lungs, especially of the right. The apex of the right lung posteriorly showed a considerable cavity. The other viscera were healthy.

Case 3.—Charles S., æt. 45, admitted to Guy's under Mr Poland, in April 1869. The patient is a farmer. His brother died of phthisis. He has always enjoyed good health and is very temperate. For the past twelve months he has had great difficulty in

passing his urine, the stream has been very small, and he has passed blood. Complains of no pains in his loins. On 13th April, it is noted that he has a bad cough, and when examined soon after by Dr Fagge, extensive disease of both lungs was detected, with crepitation and consolidation. At the post-mortem the lungs were full of gray tubercle in an early stage, but becoming cheesy. Much cheesy pus was found in the pelvis of the left kidney, with many gray tubercles. Some caseous abscesses existed in the cortex of the kidney.

Case 4.—Eliza A., æt. 21. Has been married three years. Has had two children and one miscarriage. A fortnight before coming under treatment she began suddenly to increase in size. She felt very ill, and had much abdominal pain. The abdomen was universally dull. The urine was normal, the heart-sounds also. At the post-mortem a suppurating ovary was found, with a general tuberculosis. Numerous recent yellow tubercles were found in the lungs. The abdomen contained a large quantity of thin pus, which distended it much, and the peritoneum was covered everywhere with tubercles of exactly the same appearance as those in the lungs. The viscera were adherent to each other. No ulceration or tubercle existed in the intestinal canal. Many recent yellow tubercles were found in the Fallopian tubes.

Case 5.—Edward C., admitted into Guy's, 31st March 1869, under Dr Hilton Fagge. From my own report of the case I find that both his father and mother were healthy. No cough or consumption known in the family. He was quite well ten months ago, when he fell down stairs and struck the back of his head. This did not affect him much, and for five or six weeks he enjoyed his usual health. He then fell down in a fit, in which he bit his tongue, and was very livid. He has had an odd manner since, and has dragged his left leg when walking.

At the inspection a large tubercular mass was found in the pons. Outside this mass was a layer of gray gelatinous material, which, from Dr Moxon's report, consisted of a fibrillar and vascular matrix containing faint nucleated corpuscles. The tubercle itself was very firm, like cheese—yellowish, opaque, its outer surface vascular, and having numerous minute miliary tubercles upon it.

Case 6.—Henry W., 39, admitted into Guy's, under Dr Pavy, in September 1869. He had suffered more or less from cough for eighteen months, and had been drowsy and stupid for a fortnight. When admitted he was comatose, but some phthisical mischief at the left apex was detected.

Autopsy.—An abscess three-quarters of an inch by an inch and a half existed in front of the sternum, opposite the second costal cartilage. The brain-membranes contained much tubercular deposit and lymph. The lungs were adherent by old and firm membranes to the chest-wall at the apices. Large cavities and gray tubercle existed lower down.

Case 7.—*Miliary tuberculosis of the testis following upon chronic*

disease.—Richard C., æt. 56, in Guy's under Dr Habershon, in March 1870. At the post-mortem, made by Dr Moxon, the right pleura was found closely adherent. An old cavity with fibrous induration was also found at one apex. The lungs were stuffed with recent miliary tubercles. The prostate had a large cheesy patch in its right side. The left cord, vesicula, and epididymis were in a state of caseous inflammation, and the corresponding testis had in it a very large crop of miliary tubercles. The duct was diseased to its end in the veru montanum.

Case 8.—*Yellow tubercle with acute tuberculosis in the brain.*—Jeremiah D., æt. 7, under Dr Wilks in 1870, in Guy's. His friends give no history of any fall. He has had no discharge from the ear. He began to complain of his head seven months ago. The pia mater showed acute tubercular formation, a large cheese-like greenish mass occupied the upper right central part of the cerebellum. It had a pinkish layer outside it.

Case 9.—*Old scrofulous disease of the testis, with miliary tuberculosis.*—John B., æt. 53, under the care of Dr Habershon at Guy's Hospital. He was under Mr Bryant's care two years ago for disease of the testis. On admission he did not seem very ill, but his temperature was high. His breathing soon became difficult, and physical signs of broncho-pneumonia were found. At the autopsy, both lungs were stuffed with miliary tubercle. Recent tubercle also existed in the pericardium, intestine, liver, spleen, suprarenal capsules, and kidney. The prostate had an abscess in it at the deepest part of its tissue, on the lower aspect of the urethra. The vesiculæ seminales were suppurating and ulcerated. The epididymis in a state of caseous suppuration, and adherent to scars in the scrotum. The testis had many miliary tubercles in it, otherwise it was healthy.

Of the eight cases here detailed, 2, 5, 7, 8, and 9 are perhaps more valuable than the others, as the extension of the disease was more direct, but even in these it is quite open to any one to think that no real extension occurred at all, but that all that was found was the result of a constitutional state. Neither view admits of absolute proof; but on contrasting such cases as those given with the following one, where the disease was produced in a rabbit, probabilities would appear to be in favour of the former hypothesis.

A rabbit was inoculated in the neck, on 7th November 1867, with tubercular sputa. The animal was killed on 18th March 1868, nineteen weeks after the operation. A short distance from the puncture of the injection-syringe a large mass of cheesy material was found, and around the margin of this, spreading away for half an inch into the surrounding areolar tissue, came a large number of small miliary tubercles. No enlargement of the axillary glands had taken place. The lungs contained much tubercular matter, both caseous and miliary. The liver and cæcum also were tubercular. Here, as in cases 5, 7, and 9, acute growth of tubercle was found spreading from the margin of the yellow deposit. Many

other eases may, I believe, be explained in the same way, sueh as the extension of miliary tuberele from an ulcer in the intestine, or the lighting up of tubereulosis sceondarily to serofulous abseess in the kidney, or such as the following when they oeeur :—

From the post-mortem reeords at Guy's, No. 87, for 1870. John S., æt. 11, under Mr Poland's eare. The right hip was disorganized, and a eolleetion of pus extended up under the pelvie faseia. Death took plaee from aeute general tubereulosis.

How is this extension brought about? Dr Sanderson says, by means of the lymphatic system ; and it seems probable that this is so in *many* cases up to the very termination of the disease, and *generally* so up to a eertain stage ; but bearing in mind that the disease frequently oeeurs first in the neighbourhood of the vessels, and that when it does, it is generally rapid in its progress and universal in its distribution over the body, I believe that the vaseular system also plays an important part in its produetion. For the further elueidation of this point, it may be as well to eall to mind two or three important facts, now, I believe, very generally admitted, and by the mere statement of which the whole proeess beeomes elear :—

1*st*, That eells in the animal just as mueh as those in the vegetable world will grow and produee suceessors when transplanted from one place to another.

2*dly*, That eells in a state of over-activity seem to possess the power of indueing a like activity in neighbouring eells. Pus, for example, has this power.

3*dly*, That blood-globules, more espeeially the eolourless ones, have intimate eonnexions with the surrounding tissues, and probably escape largely into those tissues.

Remembering these points, the history of eases, sueh as I have given, would probably be sueh as the following :—

A folliele, of the intestine for example, gets ehoked with its own seeretion just as a sebaeeous gland may get elogged, a small uleer forms as a natural result, and irritant matter is eonveyed to the nearest lymphatie glands. This leads to an exaltation of funetion of the gland, eells are made more quiekly, and in proportion to the rapidity of eell-formation within it, is the unstableness of the workmanship, and new eells are sent forth whieh are but ill matured, and destined to live a more rapid round of existenee. These pass into the bloodvessels (it is supposed), and in their turn exert their influenee on the tissues. Judging from the way in which the tissues are invaded, I believe they pass out into the surrounding parts, and, growing themselves, produee a like growth in the cells with whieh they eome in eontaet. Thus, ill formed as they are, their progeny would be fashioned after the same bad model. It seems probable also that this *infection* (truly so ealled) of the whole system only takes place provided that the gland function be only slightly inereased, and somewhat permanently so,—a mere temporary activity doing no harm, while very abundant eell-growth causes a too rapid

cheesy degeneration in the gland or centre of cell-formation, and, by blocking it up, for a time arrests the general contamination of the system. In this way we might account for a tabes mesenteriea, with but slight or no growth of tubercle elsewhere.

Again, to take an instance of primary infection, such as Case 1. Its history seems to be that active cells—that is to say, cells in a state of transition, on their way to a higher, or, it may be, only a more advanced, development—are injected into, or formed in, a serous cavity. They attach themselves to the moist surface, and either grow themselves or growth is induced by their presence.

The other class (*b*) is made up of all cases of acute tuberculosis, where no existing cause in the shape of pus can be discovered. As a class, it takes in more especially tubercle in the lungs, and it will also include cases of pneumonia, hæmoptysis, and chronic bronchitis, which end in tubercular disease. Strictly speaking, however, this is not a group of which it can be said that pus is entirely absent; but though it may be present, I believe it to take no necessary part in the production of the disease.

As a typical example of the class, and as a somewhat interesting case in itself, I give a short note of a case which came under the care of Dr Rutter at the Brighton Dispensary. I am much indebted to him for his kindness in allowing me to make use of my notes of it.

Case 11.—George D., æt. 39, a brewer, came to the Dispensary, stating that he was quite well till a year ago; that up to that period he had never had a cough, or indeed any other illness. During his work he strained himself lifting a hogshead of beer. Fifteen minutes afterwards, or thereabouts, he began to spit up blood in small quantity, and this gradually increased with the cough till towards the end of the day, when he brought up a large quantity of blood (he says a quart) at one cough. He continued to spit blood for two days, but has never done so since. A week after the first hæmoptysis, he had much pain in the right side, beneath the right nipple. This lasted some time, with shortness of breath, and even still troubles him now and then. He still has a good deal of cough. His mother died with cough, æt. 40. He is strong and healthy-looking, being robust and muscular. The chest expands feebly on both sides, but more so on the left than the right, and on this side also the percussion note is of higher pitch. On auscultation he has deficient respiration at the left apex, with much submucous rhonchus and stifling of the sounds. The expiratory murmur is rather prolonged and rough. Below the right nipple the ribs are depressed towards the pleural cavity, and there is dulness on percussion. Small sharp crepitation can be heard during inspiration. There is no bronchial expiration. This patch is very localized, being only about three inches in diameter.

Note.—May 1871.—The patient ceased to attend as an out-patient, and on making inquiries for him at the brewery a few days back, I learned that he had become gradually weaker and unable to work,

and had just left the town for a consumption hospital in London, but to which he had gone was not known.[1]

Cases such as this are explained by two, I think we may venture so to call them, pathological laws.

1*st*, That, under certain conditions, continued irritation will produce, first, cell-growth in excess, and then, if hypertrophy and nutrition be not commensurate, what may be designated as purposeless growth.

2*dly*, That rapidity of transition from birth to death is in direct ratio to the rapidity of development. Just as a watch with a broken cylinder will run out a length of chain in a few seconds, which, in its sound state, it would have taken hours to accomplish; so, I apprehend, it is with cells. The shorter the period of development, the shorter will be their term of life; and though passing through exactly the same stages as a healthy and well-toned cell would do, they are set to a different time, as it were, the passage between the two poles of their existence being much accelerated. In proportion to the length of time that has elapsed, and the number of generations gone through, will be the divergence of the progeny from the original type, and the less the likelihood of reversion coming into play. Carrying these points with us to the region of tubercle, we may associate them with the following facts:—That in our lungs we possess a large secretory and excretory surface, the cells of which, from the very nature of their occupation, are especially prone to change or hurry in the cycle of their life; and that, under the abnormal conditions in which we live, irritating matter is always present in the air to produce the hurried action. This being so, we might wonder that every one is not tubercular, but that it is evident that Nature has provided us with nicely-balanced powers: thus, a slightly-increased growth is met by a slightly-increased degeneration and absorption. Destroy, however, the balance either by a constitutional state, on the one hand, or an increase of local excitement on the other, and the first law holds good. What is the result? Increased epithelial formation in the first stage, growth of adenoid tissue in the second, and, should the conditions still continue, a regular invading tuberculosis is established—a disease which, if malignancy means anything, is quite as much so as the truest cancer.

Various collateral circumstances will also act somewhat in determining the extent of pathological change. For instance, in the first stage, or that of catarrhal pneumonia, according as the irritation is applied to an extensive surface or the reverse, and the cells, so to speak, run true or erratically, will be the production of an acute lobar, a vesicular, or a caseous pneumonia. The second stage will

[1] Other cases of the same kind are detailed in the Transactions of the Clinical Society, by Drs Bäumler and Herman Weber, 1869, arts. xviii. and xxvi. See also Clinical Lectures on Pulmonary Consumption, by F. Von Niemeyer, Syd. Soc. Trans., 1870. Trousseau also, in his article on Hæmoptysis, says, "Elles appellent vers les organes réspiratoires un mouvement fluxionnaire qui peut déterminer l'évolution d'une phlégmasie plus ou moins dangereuse," etc.

depend for its production mainly on two conditions—the *tendency* to cell-change in the patient, and the chronicity or otherwise of the first stage. If the cell-growth is active, a general tuberculosis will probably be established; while, if the exciting causes alone are sufficiently persistent, adenoid formation will also take place to a more limited extent, but without probably any additional stimulus form a constitutional state; I say *probably*, because it would be impossible to demonstrate with certainty the absence of such a state, the strongest evidence that could possibly be brought forward being no more than the negative test, that the disease had not hitherto shown itself.

My belief is, then, that *all chronic pneumonic changes consist in part of adenoid formation.* This view requires corroboration. The only evidence that I shall here offer on the point is, that in five such cases I found extensive thickening of the alveolar walls, with lymphoid tissue, a condition precisely analogous to that of tuberculosis, either natural or artificial, except that the round millet-like grains were absent; and this is probably not a difference of kind, but only of degree.

We must also remember that the ordinary result of a long-standing pneumonia is a permanent induration of the lung from increase of its fibrous tissue, and in connexion with this state, the undoubted fact that miners, stone-masons, or any people living in dusty atmospheres, are frequently affected with chest disease, while after death is found, not a tubercular, but a fibroid, condition of lung. If, in such cases, the earlier condition is, as I say, one of growth in the alveolar walls, the excess of fibre-tissue found post mortem must be regarded as *lymphoid tissue become fibrous*, the corpuscles having all been utilized by the proper tissue of the wall for its own repair and growth. This is the very termination one might expect from a chronic irritation proceeding continually in hardy men. It may be said by those who blame the diathesis rather than local conditions, that tuberculosis is but rarely associated with chronic bronchitis—a class of cases in which, according to the views expressed, it ought never to be absent. That the two are so rarely found together is because the effects of the irritation are neutralized by the emphysema. The ill-aerated blood, and the semi-stagnation in the lungs, are conditions unfavourable to cell-life, and thus when tubercle does occur, it is small in quantity and shrivelled, instead of being succulent and translucent. It is, therefore, named by Dr Moxon "*starved tubercle.*" For the same reason is it, probably, that tuberculosis and heart-disease are but seldom associated.[1]

The third stage of the disease, that of spreading to neighbouring tissues, is well illustrated by the following short note of a post-mortem, made a few months back. The case was one of phthisis. The right lung had its upper lobe stuffed with tubercle; at the outer

[1] Chronic bronchitis does occasionally produce phthisis. Four such cases were lately brought before the Medical Society of London by Dr Andrew Clarke, but they are certainly exceptional.

part of its base a small adhesion, half an inch broad, had formed between it and the upper angle of the lower lobe. At this spot, and nowhere else, was the lower lobe attacked. When examined microscopically, both the lymph which formed the adhesion, and the tubercular lung itself, were in exactly the same state.

But if it is the fact that caseous and suppurating deposits are liable to set up a tuberculosis, we shall find, it may be said, in surgical wards a large amount of such disease. Is this so? Several hospital surgeons have told me that it is not so very common, and this opinion is borne out by post-mortem records, for of 147 cases of joint-disease, with prolonged suppuration, inspected at Guy's during the last seven years, I find only 33, or less than a fourth, were affected with tubercle. Facts, then, are hardly in harmony with theory. An explanation, however, of this discrepancy can be found, but for the sake of convenience it has been postponed till the formation of pus has been considered. Before now leaving this, the first division of our subject, a word must be said on the metamorphoses of tubercle, seeing that upon the opinion which is held with regard to one of these, the formative, will very much depend the value one may be inclined to attach to some of the observations that have been made. These metamorphoses are chiefly two, a formative and a retrograde change. Tubercle has long been called an unorganizable material; but it is truly no such thing: at least, I have been often struck with the fact, first pointed out to me by Dr Moxon, that tubercle may often, when examined microscopically, be seen to merge into well-formed fibre-tissue;[1] and in strong support of this observation comes a fact, the truth of which I think most pathologists will admit, that it is comparatively rare to find a pair of lungs, no matter what the cause of death, in adult persons, with the apices entirely free from either tubercle or an excess of this fibrous tissue. If tubercle is absent, then a certain amount of induration exists alone, while, if it is present, except perhaps in the most acute cases, the two conditions are found together. This bears out and justifies the idea before advanced, that the two products are only modifications of tissue originally common to both.

The retrograde change is a caseous degeneration which it undergoes like most other cells of animal life. It consists essentially of a breaking-up of the interior of each globule into fatty-looking molecules, and of an ultimate disintegration of the whole mass. It may occur as the result of an atrophic or an inflammatory process.

On turning now more directly to those morbid changes with which the tuberculous state is closely associated, two difficulties arise and somewhat hamper our consideration of them. One is the desira-

[1] For observations on a similar change in tubercular omentum, see two cases recorded by Dr Payne in the Transactions of the Pathological Society, vol. xxi., 1870, p. 198. A full statement of Dr Moxon's views on this subject, and the conclusions at which he arrives, may be found in the "Medical Times and Gazette" for 1871, vol. i., in a lecture entitled "Inflammation and Tubercle." Most of those conclusions I believe I may consistently accept, at the same time that I take up a somewhat different position.

bility of avoiding repetition as far as possible; the other, that the extent of ground is large over which the subject ranges. Neither can be completely overcome, for it is impossible to treat the question in any degree fully; and of necessity the details required for the elucidation of the first part have already anticipated much that must follow. Tubercle may be examined from many standpoints; for instance, in its relation to normal nutrition, to hypertrophy, atrophy, inflammation, suppuration, or purposeless growth. Inasmuch as these questions cannot all be discussed, it will be better to contrast it more especially with *the inflammatory process* and its two principal modes of termination, viz., organization and suppuration, and then to notice a few of the many points of interest which appear to link these processes with others which belong to the class more usually designated as malignant or purposeless growths.

It would be well, before setting out on the inquiry, to define our terms; but that, unfortunately, "inflammation" hardly admits of definition, but only of description. I shall here only enter shortly upon that part of it which deals with one of the essential features of the process—the behaviour of the vessels and their contents.

Virchow, in his "Cellular Pathology," lays it down that the products of inflammation are due to the multiplication and degeneration of pre-existing cells, more especially of those of the connective tissue; but the question, "What is it that starts this proliferation?" is the one that more immediately concerns us. Older writers looked upon the whole thing as entirely an affection of the vessels, and divided it into stages, such as hyperæmia with acceleration of the blood-current, hyperæmia with retardation, stagnation, etc. After making three or four such, they came ultimately to that of rupture of the bloodvessels and extravasation of the corpuscles. Waller, Cohnheim, Charlton-Bastian, and others have come forward of late years and shown, from experiments on the lower animals, that there is a free escape of the corpuscles into the surrounding tissues *without any rupture*. The experiments of Dr Norris also rather support this view, and show, perhaps, how the process may possibly be accomplished. Whether there be any rupture or no, however, seems, as far as the result is concerned, to be but of slight importance, save that if it is so, an active agency is shown to be at work, while the mere escape of the globules by means of a laceration might, and probably would, be a passive, and therefore so far accidental, condition. All will then, I think, admit that, either by rupture or migration, the corpuscles get outside the vessels somehow, and this is the great fact to be remembered. Why is it so important? Because, when considered in connexion with what has been said of tuberculosis, it means the escape of *active* or immature material into a part where it can obtain rest and nutriment—in fact, all the conditions favourable to the perfecting of its development. Of the further stages it may be said, from what I have observed in mice, after injuring the peritoneum, and then killing them by chlo-

roform, that in three or four hours the omentum has many granular corpuscles about it which are not visible in the healthy state. In eight or ten hours similar corpuscles are seen to mingle largely with the adipose collections of the part, the normal cells of which have by this time many of them broken up into numerous small molecules. Later on still, in from twenty-four to forty-eight hours, all the elements of the tissue seem to be in an active state, and what appeared in health to be but delicate lines of connective, now swell out, and become well-marked tailed cells. The process traced thus far may, we know, go on either to organization or to pus-formation. Therefore, pus and formed material may arise from the same elements; and inasmuch as the chief product in an inflammation is cellular, they are probably both formed out of lymphoid corpuscles. That pus consists entirely of lymph-corpuscles escaped from the vessels, I am unable to believe, seeing that such large quantities will form in a few hours, and that similar corpuscles are probably largely formed at the expense of the ordinary fat-cells; neither is there any reason for binding ourselves by such an hypothesis if we recognise the law already referred to, that cells in a condition of hyperactivity possess the power of inducing a like activity in neighbouring cells. Allowing this, it may be said that the inflammatory state has for one of its chief features the escape of lymph-corpuscles into the tissues outside the vessels; that these bodies, from their nutritional activity, immediately proliferate, and by producing a like hurried action in the neighbouring tissues cause the elements of the *whole part*, not themselves alone, to partake in a rapid cell-growth. It is the rapidity which constitutes the disease, and large numbers of immature cells are its product. Since, then, cell-proliferation is common both to organized lymph and also to pus, what is the latter as distinct from an inflammatory product which stops short of suppuration? and how does this differ from the normal nutritive processes? Their respective differences may be illustrated thus:—Cell-life has three stages: 1*st*, One of development; 2*dly*, One of maintenance; 3*dly*, One of degeneration. Further, "there are facts enough to prove that the power which can be exercised in a germ is limited, so that the capacity of assuming the specific organic form cannot be communicated to an indefinite quantity of matter; and there are also enough to justify the expression that the power thus limited is, in some measure, consumed—first, in the development of every new structure; secondly, in less measure in the growth and maintenance of those already formed."[1] Healthy nutrition, then, is growth under certain restrictive influences, whereby only part of the power inherent in the germ is consumed, and energy is still reserved for development. In inflammations in which the product is organizable, the growth is excessive, and maintenance usurps the place of development; the new material is, therefore, of low formation. But inasmuch as the cell excess may vary in quantity in different cases from 1 to ∞, so will the development of the product vary; and in-

[1] Paget's Lectures on Surgical Pathology, ed. 1870, p. 119.

asmuch also as it must be supposed that there is a certain amount of force in all living things over and above that which is actually needed—a reserve force—in slight inflammations, or in robust people, the excess of cells can be fairly supplied with the power required, and thus it happens that the development is good. In suppurative inflammations the growth is in great excess of the formative power, neither development nor maintenance can be carried on, and degeneration, and indeed death, commence even at birth. But, be it remembered, the act of *dying* is not death, and though a cell be on its decline it may still be capable of much mischief; and so, I apprehend, it is with pus.

Now, it so happens that the most common, indeed nearly the sole form of cell-degeneration known, is one of fatty change—each cell becomes full of minute drops of oil, which are afterwards discharged by its breaking up. From this cause all fluids containing such bodies, or even lymph-cells, which have some close connexion with fat-tissue from their earliest formation, when in considerable quantity, have a yellowish and creamy appearance, and have been lumped together as purulent collections. We have thus come to look upon *the thing Pus* as a specific entity, which, when examined microscopically, can be recognised as such, from the fact that it is composed of rounded cells containing eccentric nuclei, etc. Further, having once recognised the presence of these bodies, we say that such fluid with its contents is incapable of passing into more permanent structures or to a higher development. But, surely, this is a most erroneous view; for just as an organizable inflammatory product may vary in its component cells from those which are perfect in form to others which are only just able to hold their own, so is it with pus, which may be anything, from a number of cells with some capability still in them of further existence, to those composed of positively dead material. The fluid being partly produced by the liquefaction of the dead cells is, of course, so far dead; but it does not follow that living corpuscles floating in it must of necessity die also; rather is it, I think, more probable that some might be able to save themselves by the disintegration of the perished ones.

The difference, then, between growth, formative inflammatory products, and suppurative ones, is mainly a question of degree—the same process, cell-proliferation, goes on in all; and so long as the part, or the whole body, is able to supply the demands made upon it for these embryonic cells, so long will there be a capability of tissue-formation, but beyond this degeneration and pus-formation will begin. It is no doubt quite true of surgical pus, if I may use the expression, when we see it fresh from an abscess, that much of it is really dead. All I wish to urge is, that what it is now, when evacuated, it was long before, as far as its characteristic cells are concerned, from the instant that they entered on the stage of fatty degeneration; but more than this—at what time each individual cell dies, or when it may be said to be positively dead, there is no evidence to show. It may also be said that, though this fatty change,

of which we have been speaking, is more especially prone to occur in lymph-glands or epithelial cells from moist surfaces, precisely the same condition may also occur in all rapidly-growing cells, or in the most highly-organized tissues, as nerve or striated muscle. Having traced the inflammatory process thus far, we may recall to mind that, in speaking of tuberculosis, two modes of onset were described —one by means of the vessels, the other by a direct stimulus to an absorbent surface. And now, again, in inflammation, I have to say that nutritional irritability may probably be brought about by the same two modes, though, strictly speaking, the two should come under one heading, seeing that we have proof only of the escape of corpuscles after the application of some irritant. Alcoholic cirrhosis would seem to supply an example of the first, and pneumonia of the second, form.

If now we compare in the lung the progress of the two diseases, pneumonia and tubercle, we find that, in both, the first stage is excessive epithelial development—that the inflammatory disease, though generally going no farther, may from thence pass on, if it be at all chronic in its course, to adenoid formation, and terminate either in a caseous pneumonia or a fibroid induration, the latter being the more common; while tubercle, always reaching the second stage, may, in its ending, become fibroid, though its disposition is usually towards softening. We may say, therefore, that the two affections, starting from the same point, usually diverge slightly in their course—the one ending in a formative, the other in a degenerative change, but that *both* not unfrequently terminate in precisely the same manner. It is often urged by those who regard pneumonia and tubercle as quite distinct diseases, that the two are antagonistic in their results—that in the one there is almost always resolution, in the other as certainly destruction of tissue; and this objection holds good of acute lobar pneumonia and tubercle. The acuteness of the attack, however, is, at the same time, the explanation of the divergence of results; the duration of the disease, and the danger of tuberculosis, being in direct ratio to each other.

Again, it is said, one always attacks the apex, the other nearly always the base of the lung; but this difference is due, I cannot but think, more to the accident of position than to the nature of the two complaints. The lower lobes are supplied with more blood—they are more directly supplied with the fresh inbreathed air, and the evacuation of the foul air is more complete than in the upper lobes, while the latter are perhaps, in addition, more fully distended and stretched. It is true that such disadvantages are, at most, but slight ones, but, small as they are, they would, on *a priori* grounds, be quite sufficient to determine that an acute disease coming by blood or air should attack the lower lobes; while that a chronic disease, or one that advances little by little, should attack that part of the lung in which the air is slightly less pure, and which is more constantly at work, is also just what we should expect.

The other objection, that tubercle is unorganizable, is, as I have

endeavoured to show, not a valid one; still, it must be said, it was partially true of the material which formed the basis of the opinion, viz., cheesy deposit. Such, no doubt, are unorganizable to the same extent that we have allowed pus to be—they both consist in great part of dead material, though by no means neeessarily entirely so.

With such views of tuberculosis and pneumonia, it is almost unnecessary to say that the distinction, *pathologically*, between a caseous pneumonia and tubercle seems purely artificial, both being a growth of adenoid material with infiltration of the lung-tissue. In what site it commenees, or whether in the earlier stages the epithelial element is more predominant than the adenoid, matters but little, if the results are the same; and I still think that the old view of what is now called caseous pneumonia, that it was a very acute tuberculosis, was anatomically correct, though perhaps clinically it may be of importance to distinguish between the two. While, therefore, the statement of Niemeyer,[1] that "the greatest danger to most phthisical patients is the development of tubercles," is certainly true, I maintain that this seeming paradox is quite as true, that *the great danger in tuberculosis is due to the formation of tubercles.* And why? Because these nodular growths have but little chance of keeping up the nutrition of their central parts, and the probability of softening down is greater than in those cases where each cell is brought into more intimate connexion with the surrounding structures.

On this point Niemeyer even does not seem to have recognised to its full extent the position he has taken up, for, after arguing in favour of "some causal connexion between the tubercles themselves and those nutritive changes in the lungs preceding their development,"[2] he proceeds further on (page 30)—"Indeed, if the doctrine that every case of phthisis consists in tuberculosis were correct, we should be obliged to admit that hæmoptysis could not very well lead to pulmonary consumption, as the exuded blood is eertainly not transformed into tubercles." But, on his own showing, hæmoptysis may cause a chronic pneumonia and tubercles develop upon it. It may still then be *possible* "that every case of phthisis consists in tuberculosis."

The close relation which inflammation and tuberculosis bear to each other is further indicated by pyæmia, which is apparently a disease consisting of an exceedingly rapid tissue-proliferation induced by the action of pus. This process may be set up by a simple surface irritation—by a gonorrhœal discharge for example—just as a pneumonia or tuberculosis may from irritation of the lung, or by an old scrofulous deposit, of which the following case is a striking instance:—

Case 12.—*Caseous abscess in the testis—Pyæmia.*—John S., æt. 26, was admitted into Guy's, under Dr Wilks, in May 1869. He came from Brighton, and had nobody with him. He seemed very drowsy, and all that could be elicited from him as

[1] Clinical Lectures on Pulmonary Consumption. By F. Von Niemeyer. New Syd. Soc., p. 11.

[2] Op. cit., p. 13.

to his history, was that he had had a fit. He had some severe epileptiform attacks while in the surgery. On 15th May he had seven fits, and he died on the 16th, rather suddenly, with a very high temperature.

Autopsy.—Face and neck marked with chronic eczema. The lungs had many patches of early lobular pneumonia. The right vesicula seminalis was in a state of caseous degeneration. The left contained recent greenish pus. The spermatic ducts came through the prostate still containing pus. The left testis was adherent, and on removing it some scrofulous-looking abscesses were cut into. The epididymis was in a condition intermediate between suppuration and softening yellow tubercle. The tubes of the epididymis were large and their walls caseous.

Over the first intercostal space was an abscess in the pectoral muscle; it had no well-defined walls.

Having now briefly reviewed some of the points in the process of inflammation, let us revert for one moment to the question, Why it is that prolonged suppurations do not so very commonly end in tuberculosis? I pointed out earlier in the paper that lymph (or at any rate exudation) corpuscles, which are closely allied to them, seem to form at the expense of the normal fat-cell. Whether they do so or not, however, is not of much consequence here, if we admit, as I think we must, that the pus-cell, or any degenerate cell, is only a lymphoid body highly charged with fat. Tubercle also is allied to the normal lymph-cell or a degenerate one, according as its development is good or bad. Practically, it is often much the same as a pus-cell, *quoad* its fat, from its earliest formation. Both pus and tubercle therefore feed upon the same material, if they both require adipose tissue for their production; and it is likely enough that if a large suppurating surface is present, draining away the fat, tubercle would have a difficulty in procuring material for its growth. On this point my own impression is, though I cannot at this moment lay my hands on facts to support it, that the spare, the lanky, and ill-formed, as a rule, have a more chronic form of phthisis than do those who are strong and well nourished; and further, when once the latter get accustomed, so to speak, to the emaciation produced by the disease, they may linger on for indefinite periods. All this, however, is in direct opposition to the clinical history of such patients, which teaches us that they do better on cod-liver oil and on a fat diet than on any other plan of treatment. I am, however, by no means sure that fats are suitable to *all stages* of the disease indiscriminately. It is possible that even harm may be done in the early stages of tuberculosis by their administration, while later on, when emaciation has proceeded to any extent, by their beneficial action on the general health they might react in a manner favourable to the patient upon the growth of the disease.

As to the connexion of scrofula with the maladies of which we have been speaking, it was formerly held, and is still, I believe, by many distinguished pathologists, that the scrofulous and tubercular

are distinct diatheses. The facts and experiments enumerated here afford but little support to such a distinction. On the contrary, the scrofulous temperament is pre-eminently a cascous or suppurative one, and it has been my endeavour to show that caseation and tuberculosis go hand in hand. As to Virchow's definition, that tubercle arises from proliferation within the connective tissue, while scrofula is a glandular affection; allowing that the distinction is a real one, which it would not appear to be if the result of such proliferation may be gland-formation, it is yet true that one may give rise to the other, and if so, can they be distinct diatheses?

We have next to notice a few facts which would appear to indicate that malignant growths are possibly not very far removed from those affections of which we have been speaking—that they are apparently offshoots from the same stock, and in their progress subject to the same laws as have already been laid down.

First, then, what has been said of inflammation and tubercle, as regards their causation by external or local irritation, may with equal truth be applied to purposeless growth. Thus, continued stimulation will produce hypertrophy, then warts, and then, in some conditions, epithelioma.

It may be again enforced that *time* is an essential element in the process. If the excitement be but temporary, the cell progeny speedily returns to its former normal type; should it be continued longer, but still short of that moment at which malignancy begins, the tendency is still to revert, but the time that must elapse between the cessation of the irritation and the re-attainment of the former pattern is proportionately increased; while in epitheliomas, the tendency to work back again is not noticed at all. Such growths are then characteristic in their infiltrations, or in the power they possess of modifying the nutritional force of neighbouring cells. But this case of epithelioma may be said to be a special one. Taking therefore the more general one of scirrhus or encephaloma, we find that they are of more frequent occurrence in the glandular epithelial organs, such as the breast and testis, and that, if the tumour be obtained in its earliest growth, the disease may often be found to attack principally the epithelium of the tubules. I have noticed this particularly in scirrhus of the breast; when not occurring in epithelial organs they are found in glands which are ever in a condition of activity, and consequently in a state of change. An apparent exception to this rule is found in the frequency with which bones are attacked by medullary cancer, but it is not really an exception; for, according to Dr Sanderson,[1] within the last few years abundant adenoid material has been found in the medulla of bones.

2dly, It is probable that a truly cancerous growth may commence in the lymphatics around the vessels as with tubercular disease. At least, this result seemed to have occurred in a patient whom I had an opportunity of examining, who died of cancer of the liver,

[1] Recent Researches on Artificial Tuberculosis, in their relation to the Pathology of Phthisis. Edinburgh Medical Journal, Nov. 1869.

associated with tubercle in the peritoneum. The tubercle was not what is ordinarily understood by that term. They were millet-like grains, which, when examined microscopically, were found to consist of structureless collections of cells in all stages. The earliest condition was one of growth in the lymphatic channels, others had in addition the same kind of corpuscles clustered immediately outside the lymphatic wall, which varied in number up to regular cancerous tubercles. In connexion with this case may be mentioned another of soft cancer of the lung in the Museum of the Sussex County Hospital, at Brighton, a note of which I have copied from the catalogue of specimens, by Dr Ormerod's kind permission :—

"D. 43.—Encephaloid disease of the lung, taken from a patient who died of malignant disease commencing in the lumbar glands, which subsequently became as large as hens' eggs. All the lymphatics were found infiltrated with cancerous matter. The spleen was scarcely at all enlarged. During life all the symptoms of leucocythæmia existed, white cells being detected in the blood in great abundance."

3dly, It is possible that malignant growths may be transplanted from one part of the body to another. An instance of this mode of production is recorded in the Transactions of the Pathological Society,[1] by Dr Moxon.

To strengthen further the position that cancerous growths are largely the result of local causes, may be mentioned the clinical fact that such growths are often attributed to blows received, and though such history may be vague and unsatisfactory, it ought not, I think, to be entirely set aside. Again, the time of life at which scirrhus of the breast most frequently appears (40 to 50, according to Birkett;[2] 45 to 50, according to Morrant Baker)[3], and the fact that 77 per cent. of such cases are or have been married,—these seem to suggest that the gland, having now no safety-valve in secretion for its declining force, takes on an erratic action. It is also to be noted that of 91 cases oberved by Mr Paget, 56 were in robust or good health at the time of the first appearance of the tumour, 9 others were in good health, and only 16 sickly.[4] Mr Birkett, however, in his article just referred to, could arrive at no definite conclusion as to the state of health when the tumour was first noticed.

If, then, tubercle, inflammatory products, and cancer, may each and all be produced, either by a local irritation or erratic development on the part of the ordinary lymph-corpuscle, in what do they differ from one another—for this they certainly do widely, both pathologically and clinically? In answer to this question, it can only be said, that they differ in the life-history of their ultimate particles. Thus, malignant growths possessing a large surplus of force expend it entirely in reproductive processes, while inflam-

[1] Vol. xx. p. 28. 1868-69.
[2] Diseases of the Breast, in Holmes's System of Surgery.
[3] Contributions to the Statistics of Cancer. Medico-Chirurg. Trans., vol. xlv.
[4] Op. cit., p. 638.

matory cells and tubercle have a disposition to distribute what they have in tissue-formation or an approach to it. The more rapid the act in each case, the less perfect will be the work done, and the more likelihood of the occurrence of a degenerative change or a caseous transformation. Other conditions will also come into play, such as the habit of the patient, the situation of the diseased part, the degree of irritation, the extent of surface upon which it is exercised, and the blood-supply to the part, whether copious or otherwise; these, again, will modify in each the result, and, in place of formed tissue or active growth, produce pus or give rise to a process of withering.

Nothing has been said of what are called innocent tumours, because, from the standpoint we have taken, such growths are much more nearly allied to the normal structures of the body than either pus, or tubercle, or cancer *as we see them*. It can only be said now, that, inasmuch as they are abnormal only by position, or the predominance of one particular tissue over another, they fall quite properly into the class of hypertrophies.

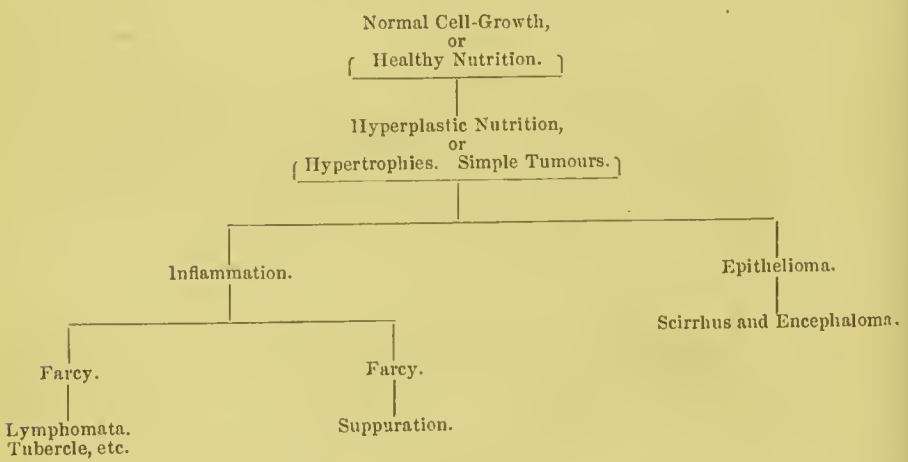
The question of multiple growths, or those in which two or more different tissues foreign to the part are found in any one organ, as enchondroma and encephaloid disease in the testicle, are not so easily dealt with, though the difficulties are such as may possibly be explained when considered in connexion with what has been put forward in this paper.

When inquiring into the nature of these morbid products, the question of *tendency* on the part of the patient has of necessity been often raised. It will not be out of place now to say that, while arguing on the side of an extrinsic factor *in all cases*, it is at the same time admitted that this would be as nothing without a soil in which it could germinate. What I wish to suggest is, that instead of using the term *diathesis* in a limited sense, as proper only to a few, it should be made universal in its application, and only variable in degree. This diathetic condition I suppose to be a proneness on the part of the whole organism, or of single cells, to degenerate by a too rapid rate of living. Believing this, I cannot think that there is any habit of body in which it would be *impossible* to produce a tuberculosis, any more than that there is one in which an inflammation could not be set on foot, while in both cases the production of disease would be infinitely easier of accomplishment in some people than in others.

But, it will be said, if you acknowledge a certain tendency, and allow that it exists in some persons more than in others, you admit an unknown quantity into your calculation, and leave us very much in the position in which we were before. Is this so? Must we not, if we acknowledge the necessity of a combination of conditions for the causation of disease, allow also that, by modifying or removing one factor, we render inoperative the action of the other? and, if so, is not a hitherto very hopeless class of cases brought more nearly into the region of the preventible?

Whether we shall ever be sensible enough as individuals to believe this, and by acting on our belief endeavour to keep dust and smoke and all other abominations from giving us tuberculosis, remains still to be proved.

In conclusion, I have thought it advisable to draw out a table which will perhaps aid in explaining more clearly than is done in the text the gist of the whole essay. This is merely as a matter of convenience. By so doing, I do not mean to imply that any scheme, however wide in its extension, is so comprehensive as to embrace all cases occurring in actual practice. On the contrary, while attempting to classify, one of the chief objects of my paper has been also to urge, that we cannot always isolate the diseases of which it has treated, and say *this* is certainly tubercle and *that* pneumonia. There will come intervening tracts whose ownership is doubtful; and it is by these intermediate links we learn a true pathology. Possibly, some whose opinion I much value may think any attempt at classification a step in a backward direction;—let me then remind such that one of the best of our living authors has said, "When it once comes to thinking, good-bye to anything like strict agreement amongst men." Until then, all doubtful points have been reduced to matter of fact; and scope is no more left for inquiry, so long is every one who honestly thinks his conclusions based upon sufficient premises entitled to his own opinion.



It now only remains for me to thank the members of the staff at Guy's Hospital, and Drs Ormerod and Rutter of Brighton, for having so kindly placed their cases at my disposal. Without these the paper would have been valueless.

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